REMARKS

The Present Invention

The present invention pertains to isolated immunogenic peptides, compositions thereof, and methods of using the same.

The Pending Claims

Claims 100-137 are currently pending, of which claims 100-115 are directed to the isolated immunogenic peptides and derivatives thereof, while claims 116 and 117 are directed to compositions comprising the same, and claims 118-137 are directed to methods of using the compositions.

The Office Action

The Office has treated the election of Group I, which encompasses claims directed to peptides from the region containing amino acids 56-70, as an election without traverse. Claims 65 and 73 have been objected to because of the use of the term "The" as the first word of independent claim 65. Claims 64, 66, 69, 70, 72, 74, 77, 78, 80, 81, 83, 84, 86, 87, 89, and 90 have been rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking description and enablement. Claims 64-67, 69, 70, 72-75, 77, 78, 80, 81, 83, 84, 86, 87, 89, 90, and 94-99 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Claims 64, 69, and 80 have been rejected under 35 U.S.C. § 102 (e) as allegedly anticipated by U.S. Patent No. 5,679,511 (the '511 patent). Reconsideration of these objections and rejections is hereby requested.

The Amendments to the Specification and Claims

The Sequence Listing has been amended to include SEQ ID NO: 39, which is incorporated by reference in the specification at, for example, page 8, line 21. Claims 64-67, 69, 70, 72-75, 77, 78, 80, 81, 83, 84, 86, 87, 89, 90, and 94-99 have been canceled. Applicants reserve the right to pursue any canceled subject matter in a continuation, continuation-in-part, divisional, or other application. Cancellation of any subject matter should not be construed as abandonment of that subject matter. Claims 100-137 have been added and are supported by the specification at the following exemplary instances:

Claims	Examples of Support in Specification
100-111	Figures 4-6 and 8-12
112-113	Page 35, line 8, through page 36, line 7, page 44, lines 1-19, and page 45, line 33, through page 46, line 4
114 and 115	Page 27, line 19, through page 28, line 2
116 and 117	Page 18, line 33, through page 21, line 16
118-137	Page 17, line 25, through page 18, line 32, and page 19, line 4

No new matter has been added by way of these amendments. Separate documents setting forth the precise changes to the specification and claims, as well as the text of all pending claims, are enclosed herewith.

Discussion of the Election without Traverse

Applicants would like to thank Examiner DeCloux for discussing the oral election of Group I, which encompasses claims directed to peptides from the region of SEQ ID NO: 39 containing amino acids 56-70. Applicants appreciate that Examiner DeCloux will allow the prosecution of peptides from the region of SEQ ID NO: 39 containing amino acids 448-462, in addition to the peptides from the region of SEQ ID NO: 39 containing amino acids 56-70, since both sets of peptides are derived from the same amino acid sequence, namely, that of the human tyrosinase protein.

Discussion of the Objection to the Claims

Claims 65 and 73 have been objected to because the use of the term "The" as the first word of claim 65, which is an independent claim, is allegedly informal. Applicants point out to the Office that these claims have been canceled. Furthermore, Applicants point out that all of the newly presented independent claims begin with the term "A" or "An". Therefore, this objection is believed to be moot.

Discussion of the Rejection under U.S.C. § 112, first paragraph

Claims 64, 66, 69, 70, 72, 74, 77, 78, 80, 81, 83, 84, 86, 87, 89, and 90 have been rejected under Section 112, first paragraph, as allegedly lacking description. This rejection is traversed for the reasons set forth below.

The Office specifically alleges that, although the specification describes immunogenic peptides *consisting* of any of SEQ ID NOs: 1-5, the specification does not

adequately describe peptides *comprising* 9 amino acids of any of SEQ ID NOs: 1-5 (emphasis added). Applicant points out to the Office that peptides comprising 9 amino acids of any of SEQ ID NOs: 1-5 are adequately described at, for example, Figures 6, 7, and 9. In particular, SEQ ID NOs: 18, 19, 20, 24, and 29 are examples of such peptides. Furthermore, Applicants maintain that immunogenic peptides can be 9 amino acids in length (see, the specification at, for example, page 9, lines 2-8), contrary to what Janeway et al. teaches (see Janeway et al., Molecular Immunobiology 1999, page 122).

However, in order to advance prosecution and not in acquiescence of the rejection, claims 64, 66, 69, 70, 72, 74, 77, 78, 80, 81, 83, 84, 86, 87, 89, and 90 have been cancelled. Moreover, all of the newly presented claims are directed to peptides *consisting essentially* of amino acids 56-70 or amino acids 448-462 of SEQ ID NO: 39, or a derivative of either of the foregoing, or to peptides *consisting* of specific amino acid sequences of SEQ ID NO: 39 (emphasis added). The instant specification adequately describes the inventive peptides at, for example, Figures 4-6 and 8-12.

The Office contends that the scope of claims 72, 74, 77, and 78 is too broad, alleging that, because the instant specification discloses that the immunogenic peptides of the rejected claims are presented by specifically HLA-DRB1*0401, the above claims should, therefore, encompass only this particular MHC molecule. Applicants point out to the Office that it is generally known in the art that multiple MHC molecules can bind to and, thus, present a given antigenic peptide (see Chicz, R.M. et al. (1993), *J. Exp. Med.* 178, 27-47; and Malcherek, G. et al. (1995), *J. Exp. Med.* 181: 527-536, which are incorporated into the instant application by reference), such that the antigenic peptide could be linked to any one of many MHC molecules, which bind to the peptide, in order for the peptide to be presented to a T lymphocyte. Applicants direct the Office's attention to the specification at page 45, line 33, through page 46, line 4, which states that "[t]he utility of these peptides in the prophylaxis and/or therapy of melanoma may not be limited to patients expressing the Class II MHC molecule DRB1*0401, as Class II-restricted peptides are often capable of binding to more than one Class II molecule." Furthermore, the Office even admits to the fact that more than one MHC molecule can bind to tyrosinase, as it states that "Tyrosinase appears to be an antigen recognized [by] a variety of MHC molecules" (see the top of page 6 in Paper No. 35). Even though the data provided in the specification are directed to tyrosinase binding to HLA-DRB1*0401, the invention should not be limited to this MHC molecule only, since it is likely that other MHC molecules will bind to the present inventive tyrosinase peptides, and it would require only routine experimentation to identify these other MHC molecules. Such routine experiments are taught in the specification at, for example, page 44, lines 1–20.

With the above said, Applicants point out that claims 72, 74, 77, and 78 have been cancelled in favor of claims 114 and 115. Applicants submit that newly presented claims 114 and 115, which are directed to immunogenic peptides linked to an MHC Class II molecule, are adequately described in the specification, at for example, page 27, line 19, through page 28, line 2.

In view of the foregoing, Applicants submit that the claimed invention is adequately described in the specification, and the scope of the newly presented claims is not overly broad. Therefore, Applicants request that the rejection under Section 112, first paragraph, be withdrawn.

Claims 64, 66, 69, 70, 72, 74, 77, 78, 80, 81, 83, 84, 86, 87, 89, and 90 have been rejected under Section 112, first paragraph, for allegedly lacking enablement. The Office specifically contends that the specification does not enable one of ordinary skill in the art to make and/or use peptides comprising a 9 amino acid segment of a sequence selected from the group consisting of SEQ ID NOs: 1-5. Applicants maintain that the specification is replete with guidance as to how to make and/or use such peptides (see, for example, page 17, line 25, through page 18, line 32, page 22, line 5, through page 28, line 27, and page 43, lines 5-13). However, in order to advance prosecution and not in acquiescence of the rejection, Applicants have canceled claims 64, 66, 69, 70, 72, 74, 77, 78, 80, 81, 83, 84, 86, 87, 89 and 90. Applicants point out that peptides comprising a 9 amino acid sequence selected from the group consisting of SEQ ID NOs: 1-5 are not within the scope of the newly presented claims. Therefore, this rejection is believed to be moot.

Claims 66, 67, 89, and 90, which are directed to methods of preventing or treating melanoma comprising administering at least one of the inventive peptides, have been rejected for allegedly lacking enablement. Specifically, the Office contends that only *in vitro* data demonstrating the ability of the peptides to stimulate TILs from patients is provided in the instant specification, and that no examples of administering a peptide of the present invention to mammals are provided. Applicants traverse this rejection for the reasons set forth below.

Applicants point out to the Office the Manual of Patent Examining Procedure (M.P.E.P.), Section 2107.03, Subsection I, which states the following:

> "As a general matter, evidence of pharmacological or biological activity of a compound will be relevant to an asserted therapeutic use if there is a reasonable correlation between the activity in question and the asserted utility...An applicant can establish this reasonable correlation by relying on statistically relevant data documenting the activity of a compound or

> compositions, arguments or reasoning, documentary evidence (e.g., articles in scientific journals), or any combination thereof. *The applicant does not have to prove that a correlation exists between a particular activity and an asserted therapeutic use of a compound as a matter of statistical certainty, nor does he or she have to provide actual evidence of success in treating humans where such a utility is asserted. Instead, as the courts have repeatedly held, all that is required is a reasonable correlation between the activity and the asserted uses.*" (emphasis in italics added).

Applicants assert that a reasonable correlation between the ability to stimulate $CD4^+$ T lymphocytes *in vitro* and the ability to prevent or treat melanoma does, in fact, exist. Furthermore, the specification is replete with guidance as to how to administer to a mammal a peptide of the present invention, or a composition comprising the same, at, for example, page 19, line 13, through page 28, line 27. Contrary to what the Office contends, Applicants submit that it would not require undue experimentation for one of ordinary skill in the art to practice a method of preventing or treating melanoma. Rather these experiments would be considered routine experimentation. Furthermore, although Rosenberg, *Immunol. Today*, 18:178 (1997) discloses that "only TILs, [which recognize the tyrosinase antigen and which are] restricted by HLA-A24[,] have been shown to mediate tumor regression *in vivo,*" this does not mean that HLA-A24 is the *only* MHC molecule by which TILs specific to the Tyrosinase antigen are restricted. Other MHC molecules could mediate tumor regression *in vivo,* but these molecules have not been identified yet.

However, to advance prosecution and not in acquiescence of the rejection, claims 66, 67, 89, and 90 have been cancelled. New claims directed to methods of inducing $CD4^+$ T lymphocytes to respond to melanoma have been added and are supported by the specification at, for example, page 17, line 25, through page 18, line 32, and page 19, line 4.

Claims 96 and 97 have been rejected under Section 112, first paragraph, for allegedly lacking enablement, since Figure 6 allegedly demonstrates that the peptides of SEQ ID NOs: 18, 19, and 24 are not recognized by $CD4^+$ T lymphocytes. Applicants contend that the peptide of SEQ ID NO: 18 demonstrated high affinity binding to the MHC Class II molecule, HLA-DRB1*0401 (see Topalian et al., *J.E.M.* 183: 1965-1971 (1996)), which is indicative of its ability to be recognized by $CD4^+$ T lymphocytes, and the peptide of SEQ ID NO: 19 demonstrated some ability to induce a T lymphocyte immune response, as well as some degree of binding to HLA-DRB1*0401. Therefore these peptides do demonstrate the ability to stimulate $CD4^+$ T lymphocytes, and are,

therefore, enabled. Applicants point out that, although claim 96, which is directed to the peptides of SEQ ID NOs: 18 and 19, has been cancelled, peptides of these sequences are within the scope of pending claim 106. In contrast to the peptides of SEQ ID NOs: 18 and 19, the peptide of SEQ ID NO: 24 neither demonstrated high affinity binding to HLA-DRB1*0401 nor stimulated GM-CSF secretion to any appreciable extent. Therefore, claim 97 which is directed to the peptide of SEQ ID NO:24, has been canceled.

In view of the foregoing, Applicants submit that the peptides of the pending claims are enabled. Therefore, Applicants request that the rejection under Section 112, first paragraph, be withdrawn.

Discussion of the Rejection under U.S.C. § 112, second paragraph

Claims 64-67, 69, 70, 72-75, 77, 78, 80, 81, 83, 84, 86, 87, 89, 90, and 94-99 have been rejected under Section 112, second paragraph, for allegedly being indefinite. This rejection is traversed for the reasons set forth below.

The Office specifically contends that claim 92 is indefinite for reciting the phrase "wherein the Q at position 1 is absent" and further contends that claims 64-67, 69, 70, 72-75, 77, 78, 80, 81, 83, 84, 86, 87, 89, 90, and 94-99 are indefinite for reciting the phrase "An isolated Major Histocompatibility Complex Class II immunogenic peptide". Applicants point out to the Office that all of these claims have been canceled. Furthermore, since none of the newly presented claims recite such phrases, Applicants submit that the pending claims are definite.

In view of the foregoing, the rejection under Section 112, second paragraph, is rendered moot. Therefore, Applicants request that this rejection be withdrawn.

Discussion of the Rejection under U.S.C. § 102(e)

Claims 64, 69, and 80 have been rejected under Section 102(e) as allegedly anticipated by U.S. Patent No. 5,679,511 (herein referred to as the '511 patent). In particular, the Office alleges that the '511 patent teaches a sequence (SEQ ID NO: 10) which *comprises* SEQ ID NO: 1 and SEQ ID NO: 2 of the instant application (emphasis added). This rejection is traversed for the reasons set forth below.

Applicants point out to the Office that claims 64, 69, and 80 have been canceled. Furthermore, all of the pending claims directed to immunogenic peptides (claims 100-118) recite either "consisting essentially of" or "consisting of" the specified amino acid sequences, which are about 15 amino acids long. In contrast, SEQ ID NO: 10 of the '511 patent is a sequence, which comprises greater than 500 amino acids. As the '511 patent

does not point out any particular fragment of SEQ ID NO: 10, the immunogenic peptides of the pending claims are not anticipated by the '511 patent.

In view of foregoing, Applicants submit that the '511 patent does not anticipate any of the peptides of the newly presented claims. Therefore, Applicants hereby request that the rejection under Section 102(e) be withdrawn.

Conclusion

The application is considered to be in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

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Date: November 18, 2002
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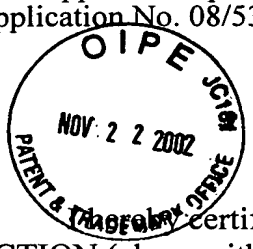
In re Appln. of Topalian et al.
Application No. 08/533,895



CERTIFICATE OF MAILING

I hereby certify that this AMENDMENT AND RESPONSE TO OFFICE ACTION (along with any documents referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: U.S. Patent and Trademark Office, Box Sequence, P.O. Box 2327, Arlington, VA 22202.

Date: Nov. 18, 2002 Kathleen M. Grentz

PATENT
Attorney Docket No. 219490
DHHS Ref. No. E-221-95/0

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Topalian et al.

Art Unit: 1644

Application No. 08/533,895

Examiner: A. DeCloux

Filed: September 26, 1995

For: MHC CLASS II RESTRICTED MELANOMA ANTIGENS AND THEIR USE IN THERAPEUTIC METHODS

AMENDMENTS TO THE SPECIFICATION AND CLAIMS
MADE IN RESPONSE TO OFFICE ACTION DATED JUNE 17, 2002

(Deletions are indicated by brackets,
while insertions are indicated by underlining)

Amendments to the claims:

64-67. Cancelled

69. Cancelled

70. Cancelled

72-75. Cancelled

77. Cancelled

78. Cancelled

80. Cancelled

81. Cancelled

83. Cancelled

84. Cancelled

86. Cancelled

87. Cancelled

89. Cancelled

90. Cancelled

94-99. Cancelled

100. (New) An isolated immunogenic peptide consisting essentially of amino acids 56-70 of SEQ ID NO: 39 or amino acids 448-462 of SEQ ID NO: 39, or a derivative of either of the foregoing, wherein the amino acid sequence of the derivative is at least 85% identical with the immunogenic peptide, wherein the immunogenic peptide or derivative thereof is recognized by a $CD4^+$ T lymphocyte, which is restricted by a Major Histocompatibility Complex (MHC) Class II molecule.

101. (New) The immunogenic peptide of claim 100, wherein the peptide consists essentially of amino acids 56-62 and 64-70 of SEQ ID NO: 39 and amino acid 63 of SEQ ID NO: 39 is substituted with a valine. OK

102. (New) The immunogenic peptide of claim 100, wherein the peptide consists essentially of amino acids 56-64 and 66-70 of SEQ ID NO: 39 and amino acid 65 of SEQ ID NO: 39 is substituted with a valine. OK

103. (New) The immunogenic peptide of claim 100, wherein the peptide consists essentially of amino acids 448-450 and 452-462 of SEQ ID NO: 39 and amino acid 451 of SEQ ID NO: 39 is substituted with a phenylalanine. OK

104. (New) The immunogenic peptide of claim 100, wherein the peptide consists essentially of amino acids 448-455 and 457-462 of SEQ ID NO: 39 and amino acid 456 of SEQ ID NO: 39 is substituted with a valine. OK

105. (New) The immunogenic peptide of claim 100, wherein the peptide consists essentially of 450-455 and 457-462 of SEQ ID NO: 39 and amino acid 456 is substituted with a valine. OK

106. (New) The immunogenic peptide of claim 100, wherein the peptide is a peptide selected from the group consisting of:

(A) a peptide consisting essentially of amino acids 56, 57, and 59-70 of SEQ ID NO: 39 and amino acid 58 of SEQ ID NO: 39 is substituted with a phenylalanine or a valine; and

(B) a peptide consisting essentially of amino acids 448 and 450-462 of SEQ ID NO: 39 and amino acid 449 of SEQ ID NO: 39 is substituted with a phenylalanine or a glutamine;

107. (New) The isolated immunogenic peptide of claim 100, wherein the peptide consists of amino acids 56-70 of SEQ ID NO: 39.

108. (New) The isolated immunogenic peptide of claim 100, wherein the peptide consists of amino acids 448-462 of SEQ ID NO: 39.

109. (New) The isolated immunogenic peptide of claim 100, wherein the peptide consists of amino acids 57-70 of SEQ ID NO: 39.

110. (New) The isolated immunogenic peptide of claim 100, wherein the peptide consists of amino acids 449-462 of SEQ ID NO: 39.

111. (New) The isolated immunogenic peptide of claim 100, wherein the peptide consists of amino acids 450-462 of SEQ ID NO: 39.

112. (New) The immunogenic peptide of claim 100, wherein the MHC Class II molecule is Human Leukocyte Antigen (HLA)-DR.

113. (New) The immunogenic peptide of claim 112, wherein the HLA-DR is HLA-DRB1*0401.

114. (New) The immunogenic peptide of claim 100 linked to an MHC Class II molecule, or a portion thereof.

115. (New) The immunogenic peptide of claim 114, wherein the portion of the MHC Class II molecule is the β chain of the MHC Class II molecule.

116. (New) A composition comprising an immunogenic peptide of claim 100.

117. (New) A composition comprising an immunogenic peptide of claim 114.

118. (New) A method of inducing $CD4^+$ T lymphocytes to respond to melanoma, which method comprises:

(i) contacting antigen presenting cells with a composition of claim 116 *in vitro*, and

(ii) simultaneously or subsequently exposing $CD4^+$ T lymphocytes to the antigen presenting cells *in vitro*,

whereupon the $CD4^+$ T lymphocytes are induced to respond to melanoma.

119. (New) The method of claim 118, wherein the $CD4^+$ T lymphocytes are obtained from a host and the method further comprises:

(iii) administering the $CD4^+$ T lymphocytes to the host.

120. (New) The method of claim 119, wherein the host is a mammal.

121. (New) The method of claim 120, wherein the mammal is a human.

122. (New) The method of claim 119, wherein the antigen presenting cells are obtained from the host.

123. (New) A method of inducing $CD4^+$ T lymphocytes in a host to respond to melanoma, which method comprises:

(i) contacting antigen presenting cells with a composition of claim 116 *in vitro*, and

(ii) subsequently exposing $CD4^+$ T lymphocytes in the host to the antigen presenting cells by administering the antigen presenting cells to the host,

whereupon the $CD4^+$ T lymphocytes in the host are induced to respond to melanoma.

124. (New) The method of claim 123, wherein the host is a mammal.

125. (New) The method of claim 124, wherein the mammal is a human.

126. (New) The method of claim 123, wherein the antigen presenting cells are obtained from the host.

127. (New) A method of inducing $CD4^+$ T lymphocytes in a host to respond to melanoma, which method comprises administering the composition of claim 116 to the host, whereupon the $CD4^+$ T lymphocytes in the host are induced to respond to melanoma.

128. (New) A method of inducing $CD4^+$ T lymphocytes to respond to melanoma, which method comprises:

(i) contacting antigen presenting cells with a composition of claim 117 *in vitro*, and

(ii) simultaneously or subsequently exposing $CD4^+$ T lymphocytes to the antigen presenting cells *in vitro*,

whereupon the $CD4^+$ T lymphocytes are induced to respond to melanoma.

129. (New) The method of claim 128, wherein the $CD4^+$ T lymphocytes are obtained from a host and the method further comprises:

(iii) administering the $CD4^+$ T lymphocytes to the host.

130. (New) The method of claim 129, wherein the host is a mammal.

131. (New) The method of claim 130, wherein the mammal is a human.

132. (New) The method of claim 128, wherein the antigen presenting cells are obtained from the host.

133. (New) A method of inducing $CD4^+$ T lymphocytes in a host to respond to melanoma, which method comprises:

(i) contacting antigen presenting cells with a composition of claim 117 *in vitro*, and

(ii) subsequently exposing $CD4^+$ T lymphocytes in the host to the antigen presenting cells by administering the antigen presenting cells to the host,

whereupon the $CD4^+$ T lymphocytes in the host are induced to respond to melanoma.

134. (New) The method of claim 133, wherein the host is a mammal.

135. (New) The method of claim 134, wherein the mammal is a human.

136. (New) The method of claim 133, wherein the antigen presenting cells are obtained from the host.

137. (New) A method of inducing $CD4^+$ T lymphocytes in a host to respond to melanoma, which method comprises administering the composition of claim 117 to the host, whereupon the $CD4^+$ T lymphocytes in the host are induced to respond to melanoma.

PATENT
Attorney Docket No. 219490
DHHS Ref. No. E-221-95/0

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Topalian et al.

Art Unit: 1644

Application No. 08/533,895

Examiner: A. DeCloux

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For: MHC CLASS II RESTRICTED MELANOMA ANTIGENS AND THEIR USE IN THERAPEUTIC METHODS

PENDING CLAIMS AFTER AMENDMENTS

MADE IN RESPONSE TO OFFICE ACTION DATED JUNE 17, 2002

100. (New) An isolated immunogenic peptide consisting essentially of amino acids 56-70 of SEQ ID NO: 39 or amino acids 448-462 of SEQ ID NO: 39, or a derivative of either of the foregoing, wherein the amino acid sequence of the derivative is at least 85% identical with the immunogenic peptide, wherein the immunogenic peptide or derivative thereof is recognized by a $CD4^+$ T lymphocyte, which is restricted by a Major Histocompatibility Complex (MHC) Class II molecule.

101. The immunogenic peptide of claim 100, wherein the peptide consists essentially of amino acids 56-62 and 64-70 of SEQ ID NO: 39 and amino acid 63 of SEQ ID NO: 39 is substituted with a valine.

102. The immunogenic peptide of claim 100, wherein the peptide consists essentially of amino acids 56-64 and 66-70 of SEQ ID NO: 39 and amino acid 65 of SEQ ID NO: 39 is substituted with a valine.

103. The immunogenic peptide of claim 100, wherein the peptide consists essentially of amino acids 448-450 and 452-462 of SEQ ID NO: 39 and amino acid 451 of SEQ ID NO: 39 is substituted with a phenylalanine.

104. The immunogenic peptide of claim 100, wherein the peptide consists essentially of amino acids 448-455 and 457-462 of SEQ ID NO: 39 and amino acid 456 of SEQ ID NO: 39 is substituted with a valine.

105. The immunogenic peptide of claim 100, wherein the peptide consists essentially of 450-455 and 457-462 of SEQ ID NO: 39 and amino acid 456 is substituted with a valine.

106. The immunogenic peptide of claim 100, wherein the peptide is a peptide selected from the group consisting of:

(A) a peptide consisting essentially of amino acids 56, 57, and 59-70 of SEQ ID NO: 39 and amino acid 58 of SEQ ID NO: 39 is substituted with a phenylalanine or a valine; and

(B) a peptide consisting essentially of amino acids 448 and 450-462 of SEQ ID NO: 39 and amino acid 449 of SEQ ID NO: 39 is substituted with a phenylalanine or a glutamine;

107. The isolated immunogenic peptide of claim 100, wherein the peptide consists of amino acids 56-70 of SEQ ID NO: 39.

108. The isolated immunogenic peptide of claim 100, wherein the peptide consists of amino acids 448-462 of SEQ ID NO: 39.

109. The isolated immunogenic peptide of claim 100, wherein the peptide consists of amino acids 57-70 of SEQ ID NO: 39.

110. The isolated immunogenic peptide of claim 100, wherein the peptide consists of amino acids 449-462 of SEQ ID NO: 39.

111. The isolated immunogenic peptide of claim 100, wherein the peptide consists of amino acids 450-462 of SEQ ID NO: 39.

112. The immunogenic peptide of claim 100, wherein the MHC Class II molecule is Human Leukocyte Antigen (HLA)-DR.

113. The immunogenic peptide of claim 112, wherein the HLA-DR is HLA-DRB1*0401.

114. The immunogenic peptide of claim 100 linked to an MHC Class II molecule, or a portion thereof.

115. The immunogenic peptide of claim 114, wherein the portion of the MHC Class II molecule is the β chain of the MHC Class II molecule.

116. A composition comprising an immunogenic peptide of claim 100.

117. A composition comprising an immunogenic peptide of claim 114.

118. A method of inducing $CD4^+$ T lymphocytes to respond to melanoma, which method comprises:

(i) contacting antigen presenting cells with a composition of claim 116 *in vitro*, and

(ii) simultaneously or subsequently exposing $CD4^+$ T lymphocytes to the antigen presenting cells *in vitro*,

whereupon the $CD4^+$ T lymphocytes are induced to respond to melanoma.

119. The method of claim 118, wherein the $CD4^+$ T lymphocytes are obtained from a host and the method further comprises:

(iii) administering the $CD4^+$ T lymphocytes to the host.

120. The method of claim 119, wherein the host is a mammal.

121. The method of claim 120, wherein the mammal is a human.

122. The method of claim 119, wherein the antigen presenting cells are obtained from the host.

123. A method of inducing $CD4^+$ T lymphocytes in a host to respond to melanoma, which method comprises:

(i) contacting antigen presenting cells with a composition of claim 116 *in vitro*, and

(ii) subsequently exposing $CD4^+$ T lymphocytes in the host to the antigen presenting cells by administering the antigen presenting cells to the host,

whereupon the $CD4^+$ T lymphocytes in the host are induced to respond to melanoma.

124. The method of claim 123, wherein the host is a mammal.

125. The method of claim 124, wherein the mammal is a human.

126. The method of claim 123, wherein the antigen presenting cells are obtained from the host.

127. A method of inducing $CD4^+$ T lymphocytes in a host to respond to melanoma, which method comprises administering the composition of claim 116 to the host, whereupon the $CD4^+$ T lymphocytes in the host are induced to respond to melanoma.

128. A method of inducing $CD4^+$ T lymphocytes to respond to melanoma, which method comprises:

(i) contacting antigen presenting cells with a composition of claim 117 *in vitro*, and

(ii) simultaneously or subsequently exposing $CD4^+$ T lymphocytes to the antigen presenting cells *in vitro*,

whereupon the $CD4^+$ T lymphocytes are induced to respond to melanoma.

129. The method of claim 128, wherein the $CD4^+$ T lymphocytes are obtained from a host and the method further comprises:

(iii) administering the $CD4^+$ T lymphocytes to the host.

130. The method of claim 129, wherein the host is a mammal.

131. The method of claim 130, wherein the mammal is a human.

132. The method of claim 128, wherein the antigen presenting cells are obtained from the host.

133. A method of inducing $CD4^+$ T lymphocytes in a host to respond to melanoma, which method comprises:

(i) contacting antigen presenting cells with a composition of claim 117 *in vitro*, and

(ii) subsequently exposing $CD4^+$ T lymphocytes in the host to the antigen presenting cells by administering the antigen presenting cells to the host,

whereupon the $CD4^+$ T lymphocytes in the host are induced to respond to melanoma.

134. The method of claim 133, wherein the host is a mammal.

135. The method of claim 134, wherein the mammal is a human.

136. The method of claim 133, wherein the antigen presenting cells are obtained from the host.

137. A method of inducing $CD4^+$ T lymphocytes in a host to respond to melanoma, which method comprises administering the composition of claim 117 to the host, whereupon the $CD4^+$ T lymphocytes in the host are induced to respond to melanoma.